IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 00486-8005.US00

Applicant(s):	Richard Anthony Godwin SMITH *et al.*	Confirmation No.: 2596
App. No.:	09/936,205	Examiner: A. Rooke
Filing Date:	October 29, 2001	Group Art Unit: 1656
Title:	ORGAN TRANSPLANT SOLUTIONS CONTAINING CONJUGATES OF SOLUBLE PEPTIDIC COMPOUNDS WITH MEMBRANE-BINDING	

United States Patent and Trademark Office
Randolph Building
401 Dulany Street
Alexandria, VA 22314

DECLARATION OF RICHARD ANTHONY GODWIN SMITH

I, Richard Anthony Godwin Smith, do hereby declare as follows:

1. At the time of the invention, I was the Chief Scientific Officer for Adprotech Ltd., and a co-inventor named on the captioned application.

2. I received my doctorate in 1974 from Oxford University. I have been engaged in research in the fields of biochemistry, molecular biology and protein engineering for over 30 years. A copy of my *curriculum vitae* is attached at **Tab 1.**

3. I have reviewed the captioned application and the office actions issued by the examiner dated December 29, 2009 (Paper No. 20091217). I provide this declaration to explain the differences between the flush storage solution (for example, SOLTRAN) and transplant solutions known in the art, and the effect those differences that would be expected to have.

The claimed invention is very different in that the recited flush storage solution (*e.g.*, SOLTRAN) is being used in an entirely different context, namely as a delivery vehicle for the soluble derivative to be carried to where it is needed in the organ. Thus, a flush storage solution must be such that the activity of the soluble derivative will be maintained

and delivered to the sites in the organ where it is needed. I submit that it is not obvious to a person skilled in the art that such a benefit would be obtainable.

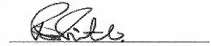
4. Typical transplant solutions at the time contained glutathione, for example, the University of Wisconsin solution. The active agent of this invention requires disulfide bonds to maintain the link between the complement inhibitor and the membrane anchor and if these links are broken, then the complement inhibitor is no longer anchored to the membrane and can be lost from the perfused organ upon restoration of blood flow to the transplanted graft.

Thus, including glutathione in transplant solutions could inappropriately reduce disulfide bonds. Therefore, typical transplant solutions, such as University of Wisconsin medium can adversely affect the construct.

5. Accordingly, one following the teachings of the field would very likely end up destroying their therapeutic soluble derivative. There was no teaching to direct the skilled person away from transplant solutions to flush solutions, particularly those lacking glutathione or similar compounds.

6. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

28 June 2010
Date


Richard Anthony Godwin Smith

CURRICULUM VITAE
2010

Richard Anthony Godwin Smith

PROFILE: Richard Smith is a specialist in protein engineering and biopharmaceuticals focused on the cardiovascular, immunotherapeutic and inflammation areas. His academic background is in chemistry and biochemistry at Oxford University and he spent 23 years in drug research and development within the Beecham Group and SmithKline Beecham (SB) where he was Director of Protein Chemistry responsible for protein target and therapeutic candidate isolation, production and analysis. While at Beecham & SB, he played a major role in the invention and development of novel thrombolytic drugs ("clotbusters'") particularly *Anistreplase* which he took from concept to market. In 1997 he co-founded a biotechnology company (Adprotech Ltd) in the Cambridge area and as its Chief Scientific Officer, built the company from 5 to 56 FTE. There, he pioneered the development of cell-targeted biopharmaceuticals including a complement inhibitor which entered Phase I and IIa clinical studies under his leadership. He became Vice President, Protein Therapeutics at Inflazyme Pharmaceuticals Ltd when the latter acquired Adprotech in 2004 and was responsible for biological operations in this Canadian publically quoted company. He is currently leading a laboratory dedicated to novel protein therapeutic agents within King's College London. He has wide experience of the worldwide pharmaceutical and biotechnology business including management of change and strategic technology assessment.

Born: 4 April 1949, Stroud, England - British Citizen
Married to Penelope Anne Clarke RGN with 3 adult children

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Education: Keble College, Oxford University
(1967-73) BA (Honours) in Chemistry (1971)
Thesis: Fluorinated Triose Phosphates
Distinction in supplementary biochemistry (Prize, 1969)
European Molecular Biology Organization training course
Cambridge University (1971)
Doctor of Philosophy, Oxford University
(completed 1973, awarded 1974)
Thesis: Photogenerated Labels for Biological Receptor Sites

Employment: Demonstrator in organic chemistry, Oxford University (1972)
(1972-2009) Beecham Pharmaceuticals Research Division (1973-89)
- Enzymologist (1973-77)
- Senior scientist, fibrinolysis research (1974-79)
- Chief biochemist, thrombosis project (1980-89)
- Manager, Modified Proteins, Biotechnology dept (1989-92)

SmithKline Beecham plc, Worldwide Biopharmaceutical R&D
- Director, Protein Chemistry (1992-96)

SmithKline Beecham plc, Molecular Screening Technologies
- Director, Therapeutic Proteins (1996-7)

Adprotech Ltd (1997-2004)
- co-founder, Board member & Chief Scientific Officer

Inflazyme Pharmaceuticals Ltd (2004-6)
- Vice President Protein Therapeutics

Department of Medicine, Cambridge University, (2006- to date)
- Honorary Senior Fellow,

Department of Medicine (Nephrology & Transplantation)
King's College London. (2007– to date)
- Director, Protein Therapeutics Laboratory, MRC Centre for Transplantation

Principal scientific achievements:

Photoaffinity labels and their application to study of the immunoglobulin antigen combining site (MRC Immunochemistry Unit, Oxford, 1972-3)

Novel penicillin transformation processes (Beecham 1974-6)

Studies on clavulanic acid (→*marketed antibiotic 'Augmentin',* Beecham 1976-8)

Invention and development of the acyl-enzyme approach to thrombolytic therapy (→ *marketed thrombolytic 'Eminase'* Beecham 1973-89)

Structural definition of fibrinolytic proteins (Beecham/SB & Oxford University,1987-93)

Development of soluble CR1 as a therapeutic anti-inflammatory agent (SB,1989-95)

Structure of IL-4 & fibronectin binding proteins (SB/Oxford,1990-4)

Invention of membrane addressin arrays & development of their therapeutic applications particularly in the form of *Mirococept* (APT070) to PhII clinical trials (Adprotech,1997-2004)

Development of novel inhibitors of complement activation (SB/Adprotech/Cardiff University/ King's College London, 1995- present)

Development of C3d-based immune adjuvants (Adprotech/Cambridge University,1998-2003)

Discovery of novel membrane-targeted antibiotics (Adprotech/Cambridge University, 2000-2004)

Scientific interests:

Protein engineering of therapeutic agents
The complement system and its role in disease and immune regulation
Molecular immunology (especially that of innate immunity)
Immunotherapeutics, anti-inflammatory agents and vaccines
Drug delivery and targeting

Non-Scientific Interests

Renaissance polyphony
Gardening in a high-calcium environment
Etymology & comparative linguistics

Other information:

Past and current member of the scientific advisory boards of several biotechnology companies
Member of the International Complement Society, the European Complement Network and the International Society on Thrombosis and Hemostasis
Maintains active scientific collaborations with academic groups in more than 10 universities and research institutes in the UK, N.America and Europe.
As CSO of Adprotech, responsible for all aspects of safety and animal care in the organisation with similar responsibilities in Canada .
Industrial or co-supervisor of 9 MSc and PhD students in UK universities (past) and 3 PhD students (current)
Occasional reviewer for The Biochemical Journal, Clinical & Experimental Immunology and other journals.
Consultant to Cambridge Enterprise Ltd and Ovasort Ltd
Awards: The Queen's Award for Technological Achievement (1967,1980 & 1991), Le Prix Galien (1991), Freedom of the City of London (1988)
UK driving licence since 1967

SCIENTIFIC PUBLICATIONS

The following is not an entirely comprehensive list of publications but it covers most significant material and is intended to illustrate areas of past and present scientific interest and expertise. Additional details of meeting presentations, posters etc are available on request. Papers in peer-reviewed journals and reviews are included along with a few abstracts dealing with work that for commercial reasons, was not subsequently published in full. Papers in submission are not included.

1. **Photoaffinity Labelling, General Protein Chemistry and Protein Engineering**

Smith RAG, Knowles J R. Aryldiazirines: potential reagents for photolabeling of biological receptor sites. **J Amer Chem Soc** 1973 95 5072-5073

Smith RAG, Knowles J R. The utility of photoaffinity labels as mapping reagents: a study of sub-populations of a specific rabbit antibody by using structurally related photoaffinity reagents. **Biochemical J** 1974 141 51-56

Smith RAG, Knowles J R. The preparation and photolysis of 3-aryl, 3-H diazirines. **J Chem Soc** 1975 (Perkin Trans.II) 686-694

Significance: the above papers are the first describing the use of diazirines as photolabels and also describe photoaffinity labelling methods since widely applied.

Garman A J, Smith RAG. The chemical modification of proteins (review). **Royal Society of Chemistry Specialist Periodical Reports,** Amino Acids, Peptides and Proteins 1982 13: 70-131 Also reviewed in vols 14-16 of this series (1983-5)

Smith RAG, Dewdney JM, Fears R, Poste G. Chemical derivatization of therapeutic proteins. (review). **Trends in Biotechnology** 1993 11: 397-403

Dodd I, Smith RAG *et al* (6 authors). Isolation and folding of proteins containing the short consensus repeat motif from an *E.coli* overexpression system. **Perspectives in Protein Enginering and Complementary Technologies** (Mayflower Press 1995)

Humphries J, Offord RE, Smith RA. Chemical methods of protein synthesis and modification. **Curr Opin Biotechnol**. 1991 2 539-543 *(review)*

Mossakowska DE , Smith RAG. Production and characterization of recombinant proteins for NMR structural studies. **Methods Mol Biol.** 1997;60: 325-335

2. **Enzyme Immobilisation**

Smith RAG. Amphipathic enzyme-polymer conjugates. **Nature (London)** 1976 262 519-520

Smith RAG. The preparation and properties of amphipathic enzyme-polymer conjugates. **Biochemical J**. 1979 181 111-115

3. **Fibrinolysis - General**

Smith RAG, Green J, Kopper P H. The purification and properties of a fibrinolytic neutral metalloendopeptidase from *Streptococcus faecalis*. **Arch Biochem Biophys** 1980 202 629-638

Dupe R J, English P D, Smith RAG, Green J. The evaluation of plasmin and streptokinase activator complexes in a new rabbit model of venous thrombosis. **Thrombosis and Haemostasis** 1981 46 528-534.

English P D, Smith RAG, Dupe R J, Green J. The thrombolytic activity of streptokinase in the rabbit. **Thrombosis and Haemostasis** 1981 46 535-537

Garman, A J, Smith RAG. The binding of plasminogen to fibrin: evidence for plasminogen-bridging. **Thrombosis Research** 1982 27 311-320

Fears R, Hibbs MJ, Smith RAG. Kinetic studies on the interaction for streptokinase and other plasminogen activators with plasminogen and fibrin. **Biochemical J** 1985 229 555-558

Smith RAG. An active-site titrant for human tissue-type plasminogen activator. **Biochemical J** 1986 239 477-479

Dodd I, Mitchell DL, Chapman CG & Smith RAG. The use of bovine fibrin-streptokinase films for the determination of recombinant human plasminogen. **Biologicals** 1992 20 197-202.

Signficance: these studies contributed to the methodological basis for the development of a new generation of thrombolytic agents.

4. **Acyl-Enzyme Thrombolytics and APSAC (anistreplase)**

Smith RAG, Dupe R J, English P D, Green J. Fibrinolysis with acyl-enzymes: a new approach to thrombolytic therapy. **Nature (London)** 1981 290 505-508

Smith RAG, Dupe R J, English P D, Green J. Acyl-Enzymes as thrombolytic agents in a rabbit model of venous thrombosis. **Thrombosis and Haemostasis** 1982 47 269-274

Staniforth, D H, Smith RAG, Hibbs M J. Streptokinase and anisoylated streptokinase.plasminogen complex: their action on haemostasis in human volunteers. **European J Clinical Pharmacology** 1983 24 751-756

Green J, Dupe R J, Smith RAG, Harris G S, English P D. Comparison of the hypotensive effects of streptokinase-human plasminogen activator complex and BRL26921 (p-anisoylated streptokinase.plasminogen activator complex) in the dog after high-dose bolus administration. **Thrombosis Research** 1984 36 29-36

Dupe R J, English P D, Smith RAG, Green J. Acyl-enzymes as thrombolytic agents in dog models of venous thrombosis and pulmonary embolism. **Thrombosis and Haemostasis** 1984 51 248-253

Dupe R J, Green J, Smith RAG. Acylated derivatives of streptokinase.plasminogen complex as thrombolytic agents in a dog model of aged venous thrombosis. **Thrombosis and Haemostasis** 1985 53 56-59

Fears R, Green J, Smith RAG, Walker P. Induction of a sustained fibrinolytic response to BRL26921 *in vitro*. **Thrombosis Research** 1985 38 251-260

Cassels R, Fears R, Smith RAG. The interaction of plasminogen activators and their acylated derivatives with fibrin and cyanogen bromide fragments of fibrinogen: relationship to fibrinolytic potency in vitro. **Biochemical J** 1987 247 395-400

Smith RAG. The non-exchange of streptokinase from anisoylated plasminogen.streptokinase activator complex and other acylated plasminogen activator complexes. **Drugs** 1987 33(3) 75-79

Hibbs M J, Fears R, Ferres H, Standring R, Smith RAG. Determination of the deacylation rate of p-anisoyl plasminogen.streptokinase activator complex (APSAC, Eminase) in human plasma, blood and clots. **Fibrinolysis** 1987 2 235-240

Smith RAG. Fibrinolysis with acyl-enzymes (review) in **Atheroma and Thrombosis** (ed V V Kakkar) Pitman Press London 1985 269-284

Green J, Harris G S, Smith RAG, Dupe R J. Acyl-enzymes: a novel class of thrombolytic agents (review) in **Thrombolysis: Biological and Therapeutic Properties of New Thrombolytic Agents** (ed D Collen et al) Churchill Livingston Edinburgh 1985 124-167

Significance: these papers describe the conception, pharmacology, pharmaceutical development and first clinical studies on the marketed thrombolytic agent anistreplase (Eminase).

5. **Third Generation Thrombolytic Agents**

Kalindjian SB, Smith RAG. Reagents for reversible coupling of proteins to the active centres of fibrinolytic enzymes. **Biochemical J.** 1987 248 409-413

Cassels R, Smith RAG. Preparation and properties of a conjugate of immunoglobulin G with the active centre of human tissue-type plasminogen activator. **Fibrinolysis** 1987 2 1889-195

Smith RAG, Esmail A F. Pharmacokinetic properties of a conjugate of tissue plasminogen activator linked through the active centre to human fibrinogen. **Fibrinolysis** 1988 2 (supp 1) 31 (abstract)

Ferres H, Smith RAG et al (7 authors). Synthesis and Fibrinolytic properties of a conjugate of urokinase with the active centre of human plasmin. **Fibrinolysis** 1988 2 (supp 1) 64 (abstract)

Robinson J H,.. Smith RAG *et al* (14 authors). A recombinant chimeric enzyme with a novel mechanism of action leading to greater potency and selectivity than tissue-type plasminogen activator. **Circulation** 1992 86 548-552

Wilson S,... Smith RAG *et al* (9 authors). The use of active centre acylation to control the pharmacokinetic profile of a recombinant chimeric plasminogen activator. **Thrombosis and Haemostasis** 1993 70 984-986

Lijnen H R, Smith RAG, Collen D. Functional properties of p-anisoylated plasmin-staphylokinase complex. **Thrombosis and Haemostasis** 1993 70 326-331

Significance: these were further contributions to the design and evaluation of novel recombinant, engineered or other thrombolytic enzymes designed to combine the best features of the currently used agents .

6. **Protein Structure Studies**

Oswald R E, Bogusky M J, Bamberger M, Smith RAG, Dobson C M. Dynamics of the multidomain fibrinolytic protein urokinase from two-dimensional NMR. **Nature (London)** 1989 337 579-582

Bogusky M J, Dobson C M, Smith RAG. Reversible independent unfolding of the domains of urokinase monitored by 1H NMR. **Biochemistry** 1989 28 6728-6735

Nowak U K, Li X, Teuten A J, Smith RAG, Dobson C M. NMR studies of the dynamics of the multidomain protein urokinase-type plasminogen activator. **Biochemistry** 1993 32, 298-309.

Li X, Smith RAG, Dobson C M. Sequential NMR assignments and secondary structure of the kringle from urokinase. **Biochemistry** 1992 31 9562-9571.

Li X, Bokman A M, Llinas M, Smith RAG, Dobson C M. Solution structure of the kringle domain from urokinase type plasminogen activator. **J. Mol Biol.** 1994 235 1548-1559

Teuten A J, Smith RAG, Dobson C M. Domain interactions in human plasminogen studied by proton NMR. **FEBS Letters** 1991 278 17-22

Redfield C,.. Smith RAG *et al* (7 authors). Secondary structure and topology of human interleukin 4 in solution. **Biochemistry** 1991 30 11029-11035

Smith L J, ..Smith RAG *et al* (7 authors). Human interleukin-4: the solution structure of a four-helix bundle protein. **J Mol Biol** 1992 224 899-904

Redfield C, Boyd J, Smith L J, Smith RAG, Dobson C M. Loop mobility in a four-helix bundle protein: 15-N NMR relaxation measurements on human interleukin-4. **Biochemistry** 1992 31 10431-10437

Teuten AJ, Broadhurst RW, Smith R.A.G, Dobson CM. Characterization of structural and folding properties of streptokinase by n.m.r spectroscopy .**Biochem. J.** 1993 290 313-9

Redfield C, Smith RAG, Dobson C M. Structural characterisation of a highly-ordered 'molten globule' at low pH. **Nature Structural Biology** 1994 1 23-29

Conejero-Lara F, Parrado J, Azuaga AI, Smith RAG, Ponting CP, Dobson CM. Thermal stability of the three domains of streptokinase studied by circular dichroism and nuclear magnetic resonance **Protein Sci.** 1996 5 2583-2591

Parrado J…Smith RAG et al (6 authors). The domain organization of streptokinase: nuclear magnetic resonance, circular dichroism, and functional characterization of proteolytic fragments. **Protein Sci.** 1996 5 693-704.

Penkett CJ…Smith RAG et al (9 authors) NMR analysis of main-chain conformational preferences in an unfolded fibronectin-binding protein. **J Mol Biol.** 1997 274 152-9

Azuaga AI….Smith RAG et al (6 authors). Expression and characterization of the intact N-terminal domain of streptokinase. **Protein Sci.** 1999 8 443-446

Penkett CJ…Smith RAG et al (8 authors) Structural and Dynamical Characterization of a Biologically Active Unfolded Fibronectin-binding Protein from Staphylococcus aureus, **Biochemistry,** 1998 87: 17054-17067 **)**

Pertinhez TA , Bouchard M, Smith RAG, Dobson CM, Smith LJ. Stimulation and inhibition of fibril formation by a peptide in the presence of different concentrations of SDS. **FEBS Letters** 2002 529 193-197

Lukacik P, …Smith R.A.G *et al* (17 authors). Complement regulation at the molecular level: the structure of Decay Accelerating Factor. **Proceedings of the National Academy of Sciences of the USA** . 2004 101 1279-1284

Leath KJ…Smith R.A.G.*et al* (8 authors). High-resolution structures of bacterially expressed soluble human CD59. **Acta Crystallographica.** 2007 F63 648-652

Significance: contributions to structural understanding of proteins of therapeutic importance.

7. **Complement Research**

Dupe R J, Smith RAG *et al* (8 authors). Utility of complement inhibition during myocardial reperfusion: pharmacology of soluble complement receptor 1. **Thrombosis and Haemostasis** 1991 65 (6) 695 (abstract).

Smith EF 3rd…Smith RA *et al (7*authors) Reduction of myocardial reperfusion injury with human soluble complement receptor type 1 (BRL 55730). **Eur J Pharmacol.** 1993 236 77-81

Gibb A L, Freeman A M, Smith RAG, Sim E. The interaction of soluble human complement receptor type 1 (sCR1, BRL55730) with human complement component C4. **Biochimica et Biophysica Acta** 1993 1180 313-320

Dodd I,...Smith RAG et al (9 authors). Overexpression in *Escherichia coli*, folding, purification and physicochemical characterisation of the first three short consensus repeat modules of human complement receptor Type-1. **Protein Expression & Purification** 1995 6 727-736

Clark NS, Dodd I, Mossakowska DE, Smith RA, Gore MG Folding and conformational studies on SCR1-3 domains of human complement receptor 1. **Protein Eng**. 1996 9 877-84.

Mossakowska D, Dodd I, Pindar W, Smith RAG. Structure-activity relationships within the N-terminal short consensus repeats (SCR) of human CR1 (C3b/C4b receptor). **Eur J Immunol**. 1999 29 1955-1965

Pratt JR……Smith RAG et al (5 authors). Effects of complement inhibition with soluble complement receptor-1 on vascular injury and inflammation during renal allograft rejection in the rat. **Am.J.Pathol.** 1996 149 2055-2066

Pratt JR, Hibbs MJ, Laver AJ, Smith RAG, Sacks SH. Allograft immune response with sCR1 intervention. **Transplant Immunol.** 1996 4 76-80

Dong J…Smith RAG et al (5 authors). Strategies for targeting complement inhibitors in ischaemia/reperfusion injury **Mol. Immunol.** 1999 36 957-963

Linton SM….Smith RAG et al (6 authors). Therapeutic efficacy of a novel membrane-targeted complement regulator in antigen-induced arthritis in the rat **Arthritis & Rheumatism** 2000 43 2590-2597

Smith GP & Smith RAG Membrane-targeted complement inhibitors **Mol.Immunol,** 2001 38 249-255

Smith RAG. Targeting anticomplement agents. **Biochem Soc Trans**. 2002 Nov;30(Pt 6):1037-41. *(review)*

Pratt JR…Smith RAG *et al (* 7 authors) Nontransgenic hyperexpression of a complement regulator in donor kidney modulates transplant ischemia/reperfusion damage, acute rejection, and chronic nephropathy. **Am J Pathol**. 2003 163 1457-65

Fraser DA, Harris CL, Smith RA, Morgan BP. Bacterial expression and membrane targeting of the rat complement regulator Crry: a new model anticomplement therapeutic. **Protein Sci**. 2002 11 2512-21

Fraser DA...Smith RA *et al (7* authors). Generation of a recombinant, membrane-targeted form of the complement regulator CD59: Activity in vitro and in vivo **J Biol Chem**. 2003 278 48921-7.

White J.. Smith RA et al (11 authors). Biological activity, membrane-targeting modification, and crystallization of soluble human decay accelerating factor expressed in E. coli. **Protein Sci**. 2004 13 2406-15.

Harris CL, Abbott RJ, Smith RA, Morgan BP, Lea SM. Molecular Dissection of Interactions between Components of the Alternative Pathway of Complement and Decay Accelerating Factor (CD55). **J Biol Chem**. 2005 280 2569-2578

Halstead SK,,Smith RA et al (6 authors). Complement inhibition abrogates nerve terminal injury in Miller Fisher syndrome.. **Ann. Neurol.** 2005 58:203-210

Hill A....Smith RA et al (12 authors). Protection of erythrocytes from human complement mediated lysis by membrane-targeted recombinant soluble CD59: A new approach to PNH therapy. **Blood**. 2006 107:2131-2137

Patel H. Smith RA, Sacks SH, Zhou W. Therapeutic strategy with a membrane-localizing complement regulator to increase the number of usable donor organs after prolonged cold storage. **J. Am Soc.Nephrol.** 2006 17:1102-1111

Omidvar N...Smith RA et al (6 authors) Expression of glycosylphosphatidylinositol-anchored CD59 on target cells enhances human NK cell-mediated cytotoxicity. **J.Immunol.** 2006 176:2915-2923

Banz Y...Smith RA et al (10 authors) Attenuation of myocardial reperfusion injury in pigs by Mirococept, a membrane-targeted complement inhibitor derived from human CR1 . **Cardiovascular Res.** 2007 76:482-493.

Peng Q...Smith RA et al (8 authors) Local production and activation of complement up-regulates the allostimulatory function of dendritic cells through C3a-C3aR interaction. **Blood.** 2008,111:2452-2461

Lachmann PJ., Smith RAG. Taking complement to the clinic: has the time finally come? **Scan. J.Immunol.** 2009 69: 471-478 (*review*)

Significance: engineering and evaluation of complement inhibitory proteins, two of which have entered clinical trials

8. **Novel Vaccines**

Barrault DV, Steward M, Cox VF, Smith RA, Knight AM. Efficient production of complement (C3d)3 fusion proteins using the baculovirus expression vector system. **J Immunol Methods**. 2005 304 158-173.

9. **Genomics and Science Management**

Dewdney JM, Smith RAG Putting a new spin on R&D assets in the pharmaceutical industry. **Drug Discovery Today** 1998 3 353-354 *(editorial)*

Smith RAG Biopharmaceuticals in the late genomic era *in* Genomics : commercial opportunities from a scientific revolution / edited by G.K. Dixon, L.G. Copping and D. Livingstone 1998, Oxford : **Bios Scientific Publishers**

Smith RAG Protein Therapeutics – new ladders up the fruit tree. **Drug Discovery World** 2001 (Spring) 65-70

10. **Other Protein Engineering**

Bowles CE…Smith RA *et al* (6 authors) Membrane reinsertion of a myristoyl-peptidyl anchored extracellular domain growth hormone receptor. **Endocrinology**. 2007;148: 824-830.

11. **Most recent issued patents** (a list of earlier patents is available on request)

Mossakowska DEI, Cox VF, Smith RAG. 2004, US 6,833,437. Complement receptor type 1 (CR1)-like sequences

Mossakowska DEI, Edge CM, Smith RAG. 2004. US 6,797,806. Fragments of CR1 and their use

Cox VF, Smith RAG, Rowling PJE. 2004, US 6,770,631 B1 Non-identical genes and their application in improved molecular adjuvants

Smith RAG, Dodd I, Mossakowska DEI. 2004, US 6,713,606. Conjugates of soluble peptidic compounds with membrane-binding agents

Smith RAG, Beeley LJ. 2001. US 6,187,751. Biologically active peptide of ob protein

Mossakowska DEI, Dodd I, Freeman AM, Smith RAG. 1999, US 5,859,223. Soluble CR1 derivatives

12. **Recent invited scientific talks**

Towards an integrated cytotopic strategy for graft modification in transplantation – complement & coagulation. XIIth European Meeting on Complement in Human Disease, Visegrad, Hungary, September 7, 2009 (s/a: Molecular Immunology 46, 2833,2009)

A Better Vancomycin: Applying Cytotopic Protein Modification Technology to the improvement of Antibiotics. UK-SE Asia Symposia on Current Strategies in Antibiotic Therapies. Biopolis, Singapore & University of Malaysia, March 17-19, 2009

A Better Vancomycin: Applying Cytotopic Protein Modification Technology to the improvement of Antibiotics. Genesis/Bioversity Conference, London, December 9, 2008

Cytotopic Pharmacology: Molecular Basis and Therapeutic Applications. November 19, 2008. University of Szeged, Hungary

Biological agents and pandemic planning. ICAV Sixth International Symposium, May 6, 2008. Peterborough, Ontario, Canada.

Making better use of Donated Organs: the Protein Chemistry solution. February 7, 2008. NIHR-Biomedical Research Centre Forum, Guy's Hospital, London UK.

Membrane-Localising Complement Inhibitors – Clinical Progress. September 9, 2007, XIth European Meeting on Complement in Human Disease. Cardiff, UK

Engineering Biologically Active Agents to Function on Membranes- adding intrinsic worth. March 9, 2007. Cambridge University Department of Chemistry, Cambridge UK